Atty. Dkt. No. 24406 Serial No. 09/673,473 Filed: November 29, 2000

REMARKS

Following entry of this amendment, claims 1, 3, 5-7 and 13-17 are present in this application. The claims have been amended in order to better clarify the subject matter sought to be protected. In addition, a corrected version of Figure 1 is being submitted to overcome the draftperson's objections thereto.

The claims have been amended in the expectation that the entry of the amendments, along with the following comments, will place the application in condition for allowance. No new matter within the meaning of 35 U.S.C. 132 is added by the above claim amendments and corrected Figure 1.

With entry of the above amendments and following remarks, Applicants respectfully submit that the claims are now in condition for allowance.

1. Objection to the Drawings

The Notice of Draftperson's Patent Drawing Review indicates that Figure 1 is objected to as containing non-uniform lines, numbers and legends. Applicants submit herewith a corrected Figure 1. The corrected figure has been amended to overcome the objection to the figure, thus removing the basis for the objection. Accordingly, Applicants respectfully request reconsideration and

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withdrawal of the objection to the Figure, as indicated on the Notice accompanying the Office Action.

2. Rejection of claims 14 and 15 Under

35 U.S.C. 112, Second Paragraph

Claims 14 and 15 stand rejected under 35 U.S.C. 112, second paragraph as being indefinite for the inclusion of the term "anxiety and related disorders" within the claims.

Applicants thank the Examiner for the helpful suggestion to overcome this rejection. Applicants have amended claims 14 and 15 to remove "and related" from the claims, as was suggested by the Examiner. In removing the phrase "and related," Applicants have removed the basis for this rejection. In addition, Applicants have removed the parenthetical examples from the claims, thus rendering the claims definite. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection.

3. Claim Objections

The Examiner has objected to claims 1, 3, 5-7 and 13-17 as containing non-elected subject matter.

Applicants have amended the claims to remove the non-elected subject matter without prejudice or disclaimer thereto. Thus,

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Applicants respectfully submit that the claims are now in condition for allowance.

CONCLUSION

In view of the foregoing, applicant respectfully requests the Examiner to reconsider and withdraw the rejection of the claims and to allow all of the claims pending in this application.

If the Examiner has any questions or wishes to discuss this matter, the Examiner is welcomed to telephone the undersigned attorney.

Respectfully submitted, NATH & ASSOCIATES PLLC

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We claim:

1. (currently amended) A compound of the formula:

$$R1$$
 $R2$
 $R3$
 $R3$
 $R1$

wherein:

R1 can be an acidic group selected from the group consisting of <u>is</u> carboxyl, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, -CH2-carboxyl, -CH2-phosphono, -CH2-phosphino, -CH2-sulfono, -CH2-sulfino, -CH2-borono, -CH2-tetrazol, and -CH2-isoxazol;

R2 ean be is a basic group selected from the group consisting of 1° amino, 2° amino, and 3° amino, quaternary ammonium salts, aliphatic 1° amino, aliphatic 2° amino, aliphatic 3° amino, aliphatic quaternary ammonium salts, aromatic 1° amino, aromatic 2° amino, aromatic 3° amino, aromatic quaternary ammonium salts, imidazol, guanidino, boronoamino, allyl, urea, thiourea;

R3 can be H, aliphatic, aromatic or heterocyclic is CH₂-thioxanthyl;

R4 can be an acidic group selected from the group consisting of <u>is</u> carboxyl, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol; and pharmaceutically acceptable salts thereof.

- 2. (withdrawn)
- 3. (original) A compound as claimed in claim 1, wherein **R2** is NH₂.
- 4. (withdrawn)

- 5. (currently amended) A process for the preparation of a compound of Formula I as claimed in claim 1, or a pharmaceutically acceptable metabolically-labile ester or amide thereof, or a pharmaceutically acceptable salt thereof, which comprises:
 - (a) hydrolyzing a compound of formula:

wherein: **R**'1 is an acidic group selected from the group consisting of carboxyl, phosphono, phosphino, sulfono, sulfino, borono, tetrazol, isoxazol, CH2 carboxyl, CH2 phosphono, CH2 phosphino, CH2-sulfono, CH2-sulfono, CH2-sulfono, CH2-borono, CH2-tetrazol, CH2-isoxazol and higher analogues thereof, or a protected form thereof, **R3** can be H, aliphatic, aromatic or heterocyclic is CH2-thioxanthyl and **R5** represents a hydrogen atom or an acyl group, and wherein preferred values for **R5** are hydrogen and (2-6C) alkanoyl groups, such as acetyl; or

(b) deprotecting and hydrolyzing a compound of formula (II b)

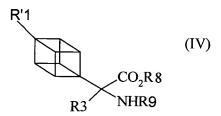
wherein: R'1 and R3 are as defined above; or

(c) hydrolyzing a compound of formula:

$$R^{'1}$$
 $R^{'1}$
 $R^{'1}$
 $R^{'1}$
 $R^{'1}$
 $N-R^{'1}$
 $N-R^{'1}$
 $N-R^{'1}$

wherein: **R6** and **R7** each independently represent a hydrogen atom, a (2-6C) alkanoyl group, a (1-4C) alkyl group, a (3-4C) alkenyl group or a phenyl (1-4C) alkyl group in which the phenyl is unsubstituted or substituted by halogen, (1-4C) alkyl or (1-4C) alkoxy, or a salt thereof, **R'1** and **R3** are as defined above; or

(d) deprotecting a compound of formula:



wherein: **R8** represents a hydrogen atom or a carboxyl protecting group, or a salt thereof, and **R9** represents a hydrogen atom or a nitrogen protecting group, **R'1** and **R3** are as defined above;

whereafter, if necessary and/or desired:

- (i) resolving the compound of Formula I;
- (ii) converting the compound of Formula I into a non-toxic metabolically-labile ester or amide thereof; and/or
- (iii) converting the compound of Formula I or a non-toxic metabolicallylabile ester or amide thereof into a pharmaceutically acceptable salt thereof.

- 6. **(original)** A pharmaceutical formulation, which comprises a compound as claimed in claim 1 and a pharmaceutically acceptable carrier, diluent or excipient.
- 7. (previously amended) A method of modulating one or more metabotropic glutamate receptor functions in a warm blooded mammal, comprising administering an effective amount of a compound of formula (I) as claimed in claim 1 to a warm blooded mammal in need thereof.
- 8. (withdrawn)
- 9. (withdrawn)
- 10. (withdrawn)
- 11. (withdrawn)
- 12. (withdrawn)
- 13. (previously added) A compound according to claim 1, wherein R1 is -COOH, R2 is -NH2, R3 is -CH₂-thioxanthyl and R4 is COOH.
- 14. (currently amended) A method of treating a neurological disease or disorder in a warm blooded mammal comprising administering an effective amount of the compound of formula (I) according to claim 1 to a warm blooded mammal in need thereof, wherein said neurological disease or disorder is selected from the group consisting of cerebral deficits subsequent to cardiac bypass surgery and grafting, cerebral ischemia, stroke, cardiac arrest, spinal cord trauma, head trauma, perinatal hypoxia, and hypoglycemic neuronal damage, Alzheimer's disease, Huntington's Chorea, amyotrophic lateral sclerosis, AIDS-induced dementia, ocular damage, retinopathy, cognitive disorders, idiopathic and drug-induced Parkinson's disease, muscular spasms, convulsions, migraine headaches, urinary incontinence, psychosis, drug tolerance, withdrawal, and cessation (i.e. opiates, benzodiazepines, nicotine, cocaine, or ethanol), smoking cessation, anxiety and related disorders (e.g. panie)

attack), emesis, brain edema, chronic pain, sleep disorders, Tourette's syndrome, attention deficit disorder, and tardive dyskinesia.

- 15. (currently amended) A method of treating a psychiatric disease or disorder in a warm blooded mammal comprising administering an effective amount of the compound of formula (I) according to claim 1 to a warm blooded mammal in need thereof, wherein said psychiatric disease or disorder is selected from the group consisting of schizophrenia, anxiety and related disorders (e.g. panie attack), depression, bipolar disorders, psychosis, and obsessive compulsive disorders.
- 16. (currently amended) The method according to any one of claims 7, 14 or 15 5, 7 or 8 wherein said compound is selected from the group of compounds consisting of

$$HO_2C$$
 CO_2H
 NH_2
 CO_2H
 HO_2C
 HO_2C

17. (previously amended) A method of treating cerebral ischemia, stroke and cardiac arrest in a warm blooded mammal comprising administering an effective amount of the compound:

to a warm blooded mammal in need thereof.

- 18. (withdrawn)
- 19. (withdrawn)
- 20. (withdrawn)
- 21. (withdrawn)